

Application No. 10/713929
Docket No. 451194-101
Amendment in Response to Office Action filed January 13, 2006
Page 2

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims of this application:

Listing of Claims:

1. (currently amended) A multi-particulate pharmaceutical dosage form of a skeletal muscle relaxant providing a modified release profile comprising a population of extended release (~~ER~~) beads,

wherein said ~~ER~~ extended release beads comprise

an active-containing core particle (~~IR (immediate release) bead~~) comprising a skeletal muscle relaxant; and

an ~~ER~~ (extended release) coating comprising a water insoluble polymer membrane surrounding said core,

wherein said dosage form when dissolution tested using United States Pharmacopoeia Apparatus 2 (paddles @ 50 rpm) in 900 mL of 0.1N HCl at 37°C exhibits a drug release profile substantially corresponding to the following pattern:

after 2 hours, no more than about 40% of the total active is released;

after 4 hours, from about 40-65% of the total active is released

after 8 hours, from about 60-85% of the total active is released; and

after 12 hours, from about 75- 85% of the total active is released;

thereby wherein said dosage form provides providing therapeutically effective plasma concentration over a period of 24 hours to treat muscle spasm associated with painful musculoskeletal conditions when administered to a patient in need thereof in humans.

Application No. 10/713929
Docket No. 451194-101
Amendment in Response to Office Action filed January 13, 2006
Page 3

2. (original) A pharmaceutical dosage form as defined in claim 1, wherein said skeletal muscle relaxant is selected from the group consisting of cyclobenzaprine, dantrolene, methocarbamol, metaxalone, carisoprodol, diazepam, pharmaceutically acceptable salts or derivatives thereof and mixtures thereof.
3. (original) A pharmaceutical dosage form as defined in claim 2 wherein said skeletal muscle relaxant is cyclobenzaprine hydrochloride and said pharmaceutical dosage form provides a maximum blood plasma concentration (C_{max}) within the range of about 80% to 125% of about 20 ng/mL of cyclobenzaprine HCl and an AUC_{0-168} within the range of about 80% to 125% of about 740 ng-hr/mL and a T_{max} within the range of 80% to 125% of about 7 hours following oral administration of a single 30 mg cyclobenzaprine HCl MR Capsule.
4. (original) A pharmaceutical dosage form as defined in claim 3 wherein the adjusted mean ratio of $CMR\ 30\ mg/CMR\ 15\ mg$ is greater than about 2 for each of AUC_{0-168} ($p < 0.001$), $AUC_{0-\infty}$ ($p < 0.001$), and C_{max} ($p < 0.001$).
5. (currently amended) A pharmaceutical dosage form as defined in claim 1 further comprising an immediate release (~~IR~~) bead population, wherein said ~~IR~~ immediate release comprise an active-containing core particle comprising a skeletal muscle relaxant and said immediate release beads when tested in a USP Type 2 Apparatus at 50 rpm in 900 ml 0.1 N HCl at 37°C release at least about 70% of the active within 30 minutes.
6. (original) A pharmaceutical dosage form as defined in claim 1, wherein said dosage form comprises only one extended release bead population.
7. (original) A pharmaceutical dosage form as defined in claim 1, wherein said water insoluble polymer is selected from the group consisting of ethers and esters of cellulose, pH-insensitive ammonio methacrylic acid copolymers, and mixtures thereof.

Application No. 10/713929
Docket No. 451194-101
Amendment in Response to Office Action filed January 13, 2006
Page 4

8. (original) A pharmaceutical dosage form as defined in claim 7, wherein said extended release coating further comprises a plasticizer.

9. (original) A pharmaceutical dosage form as defined in claim 8, wherein said plasticizer is selected from the group of triacetin, tributyl citrate, tri-ethyl citrate, acetyl tri-n-butyl citrate, diethyl phthalate, dibutyl sebacate, polyethylene glycol, polypropylene glycol, castor oil, acetylated mono- and di-glycerides and mixtures thereof.

10. (original) A pharmaceutical dosage form as defined in claim 1, wherein said water insoluble polymer membrane on the drug cores comprises from about 7% to 12% by weight of the coated beads.

11. (original) A pharmaceutical dosage form as defined in claim 7, wherein said extended release coating further comprises a water soluble polymer selected from the group consisting of methylcellulose, hydroxypropylcellulose, hydroxypropyl methylcellulose, polyethylene glycol polyvinylpyrrolidone and mixtures thereof.

12-22. (canceled)

23. (withdrawn) A multi-particulate pharmaceutical dosage form of a skeletal muscle relaxant providing a modified release profile comprising a population of extended release (ER) beads,

wherein said ER beads comprise

an active-containing core particle (IR (immediate release) bead) comprising an inert core coated with an active-containing composition consisting essentially of a skeletal muscle relaxant; and

Application No. 10/713929
Docket No. 451194-101
Amendment in Response to Office Action filed January 13, 2006
Page 5

an ER (extended release) coating comprising a water insoluble polymer membrane surrounding said active-containing core particle,

wherein said dosage form when dissolution tested using United States Pharmacopoeia Apparatus 2 (paddles @ 50 rpm) in 900 mL of 0.1N HCl at 37°C exhibits a drug release profile substantially corresponding to the following pattern:

after 2 hours, no more than about 40% of the total active is released;

after 4 hours, from about 40-65% of the total active is released

after 8 hours, from about 60-85% of the total active is released; and

after 12 hours, from about 75- 85% of the total active is released;

wherein said dosage form provides therapeutically effective plasma concentration over a period of 24 hours when administered to a patient in need thereof.

24. (new) A pharmaceutical dosage form as defined in claim 1, wherein said skeletal muscle relaxant comprises cyclobenzaprine.